REMARKS/AMENDMENTS

I. Status of Claims

Claims 1 to 12 and 14 are pending in this application. Claims 1, 3, 5, 7, 9, 11, 12 and 14 have been amended. Claim 4 has been canceled. A new claim 15 has been added. No new matter has been added with these amendments.

II. Election/restriction

The Examiner's restriction into two groups is unclear. The Applicants do not understand why the Examiner is further restricting group II with the "proviso type" statement "…when the variable Y represents heteroaryl select from pyridine thereof …, the variable A, X or R_1 independently does not represent heteroaryl thereof …, the variable A, X or R_1 independently is not substituted with heteroaryl. The Applicants respectfully request clarification of the above statement. Further, on page 4 (last paragraph) the Examiner states that "the instant case, Group I-III are drawn…" when there has been no previous discussion of a group III. The Applicants respectfully request clarification of what the Examiner means by group III. The Applicants believe that the elected species has been found allowable by the Examiner and an examination of the Markush group should be extended beyond the boundaries of the elected species.

III. Lack of Unity

The Examiner states that claims 1-12 and 14 of the present application lack unity of invention under PCT rule 13.1 and 13.2. Particularly the Examiner states that the claims lack a significant structural element qualifying as a special technical feature that defines a contribution over Marsilje et al. US 7,060,697. The Applicants respectfully disagree. In the present invention, the nitrogen containing ring of the Markush group is directly attached to the Y moiety. In contrast, the Markush group of US 7,060,697 clearly defines a $-CR_3R_4-$ linker between the Z moiety and phenyl. Further, in the present invention A is linked to the nitrogen containing ring via an alkyl linker. In contrast, the Markush group

of US 7,060,697 has the carbonyl group of A directly attached to the Z moiety. For the reasons stated above, the Applicants believe that the compounds of the present invention have significant structural elements that define them over Marsilje et al., and therefore are not lacking in unity under 37 CFR 1.475 (a).

The Examiner also states that the claims lack unity under 1.475 (b). The Applicants respectfully disagree because: claims 1 to 10 are product claims; claims 11 and 12 are methods of using the product; and claim 14 is a process for making the product. Therefore, the instant claims have unity of invention as defined by 1.475 (b)(3) which states " a product, a process specially adapted for the manufacture of the said product, and a use of said product".

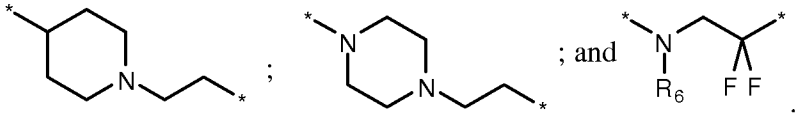
Further, the Applicants draw the Examiners attention to the International Preliminary Report on Patentability for PCT application PCT/US05/06311 (transmitted 03 April, 2006) which has no finding of lack of unity for the present invention.

IV. Claim Rejections – 35 USC §112

The Applicants have amended the claims according to the Examiners suggestions. Specifically, the Applicants have deleted "prevent" and incorporated named diseases into claims 11 and 12 to obviate the rejection. Support for these amendments can be found in the specification beginning line 24 on page 11 and in example 56, page 41.

IV. Claim Rejections – 35 USC §103

Claims 1-12 and 14 are rejected under 35 USC 103(a) as being unpatentable over Marsilje et al. US 7,060,697. The Examiner has compared the Z moiety of Marsilje et al., with the nitrogen containing ring of the Markush group of the present invention. Specifically Marsilje represents the following three groups:



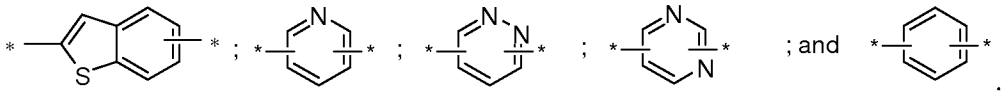
However, contrary to the Examiner's comparison, the instant claims are not represented by the groups above. Specifically, there is no $-CH_2CH_2-$ linker in the present invention. The nitrogen containing ring in the present Markush group is directly linked to the ring system defined by Y. Further, in the present invention A is linked to the nitrogen containing ring via an alkyl linker. In contrast, the Markush group of US 7,060,697 has the carbonyl group of A directly attached to the Z moiety. For these reasons, there is no inherent overlap between the compounds of Marsilje et al. and the present invention and Marsilje et al. does not teach the compounds of the present invention.

The Examiner has suggested motivation to derive the claimed compounds from Marsilje. However, the Applicants disagree that the differences between the present invention and that of Marsilje et al. are obvious in that such structural differences can change the flexibility, conformation, and physical, chemical and/or electrostatic properties of compounds. These structural differences can be all the more profound in the context of the confines of a protein binding pocket such as the EDG/S1P receptor.

V. Claim Objections

The Applicants have amended the claims to obviate the Examiner's objection and in an effort to expedite the prosecution of this application.

Y has been amended to be selected from:



Support for each of these groups can be found in the specification. Particularly, in the examples beginning on page 24 (including table 1, page 36). For example: Y is phenyl in examples 1 (page 24), 4-8 (pages 31-35), 9-30 (table 1, page 36), 32 (table 1, page 39), 36-49 (table 1, pages 39-40), 51-55 (table 1, page 41); Y is pyridine in examples 2 (page 26), 3 (page 28) and 50 (table 1, page 40); Y is pyridazine in example 31 (table 1, page 38); Y is pyrimidine in example 33 (table 1, page 39); and Y is benzo[b]thiophene in examples 34-5 (table 1, page 39).

Amendments have been made to n and m, specifically n=2 and m=3 have been deleted. Support for n=0 can be found in the specification in example 16, 17, 26, 45 (table 1, beginning page 36). Support for n=1 can be found in examples1-11, 15, 18-25, 28-43 and 46-55. Support for m=1 can be found in examples 12,14,16-7, 19, 25-6, 36-9, 41-2 and 44-5.

Amendments to X have been made such that X is defined as "a bond or is chosen from $-CH_2O-$, $-OCH_2-$, $-CH_2S-$ and C_{4-6}heteroarylene". Support for these amendments are found in the specification. X is: $-CH_2S-$ in example 52; $-CH_2O-$ in examples 1, 3-5, 8-18, 21-3, 29, 47, 49-51, 53-55; $-OCH_2-$ in examples 2, 6-7, 19-20, 24-8, 30-3 and 48; bond in examples 34-5; and heteroarylene in examples 36-46.

A new claim (claim 15) has been added to cover the compounds 1-(1H-Tetrazol-5-ylmethyl)-4-[4-(2-trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-piperidine and 1-[2-(1H-Tetrazol-5-yl)-ethyl]-4-[4-(2-trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-piperidine which are detailed in the specification as examples 30 (table 1, page 38) and 32 (table 1, page 39), respectively.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-812-1796.

Respectfully submitted,
/Scott W. Reid, Reg. No. 48,097/

Scott W. Reid, D.Phil.
Reg. No. 48,097
Agent for the Applicants

Customer No.: 29490
Phone: (858) 812 1796
Fax: (858) 812 1909